THE PREVENTIVE AND CURATIVE TREATMENT OF GAS GANGRENE BY MIXED SERUMS.

BY

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IN a paper written in 1916[1] on cases of gas gangrene treated in the Scottish Women's Hospital, Royaumont, I indicated that I had obtained some good results in a few cases where I utilized as a curative measure the anti-*perfringens* serum prepared by MM. Weinberg and Séguin at the Pasteur Institute. In these cases the infection was already established even to the stage of intoxication and septicaemia. At that time I expressed a hope that the preventive treatment of gas gangrene by serum would become as universal and as satisfactory as that of tetanus. It has been a disappointment to see how little progress has been made in this direction compared with other improvements in the treatment of war wounds, for it is practically certain that cases of gas gangrene will always occur during periods of great military activity.

Convinced by my previous experience of the curative value of serum, I determined that, should the opportunity arise, I would test also the preventive use of anti-gangrenous serum. From March 21st to September 6th, 1918, 3,660 recently wounded received their first operative treatment in the hospitals under my care, and in this short note I propose to state the results obtained.

The investigations of the flora of gas gangrene pursued by the bacteriologists who have worked in our laboratories have confirmed the observations of those scientific workers who have specially occupied themselves with the question, and it has been shown that in the majority of cases this is very complex. By the side of *B. perfringens* one finds other pathogenic microbes which cause the death of the patient. Among these are the *Vibrion septique* and the *B. oedematiens*.

The association of the streptococcus, which flourishes in increased luxuriance where the ground is prepared for it by these bacilli, is a highly important factor in the ultimate prognosis. I expected therefore to get better therapeutic results by the employment of mixed serums, or a polyvalent serum active at once against the principal pathogenic microbes of gas gangrene.

I have employed in three series of cases:

(*a*) The mixed serums anti-*perfringens*, anti-*Vibrion septique*, anti-*oedematiens*, prepared by MM. Weinberg and Séguin.

(*b*) The polyvalent serum of MM. Leclainche and Vallée.

(*c*) A combination of the two.

In a communication to the Société de Chirurgie de Paris on July 31st, 1918,[2] P. Delbet reported the results I had obtained at the Scottish Women's Hospital, Royaumont, by the preventive use of the mixed Weinberg serum, in a series of 157 cases, in which no death from gas gangrene had occurred, although 8 who had received no prophylactic dose had died from gas gangrene in the same period.

Owing to the rapidity of evolution of gas gangrene, isolation of the specific microbe in the majority of cases is not possible, and it is necessary to act energetically long before the complicated bacteriological researches necessary for the identification of the microbe have been completed. Should this, however, be possible, adequate doses of the specific serum can be given, as in the following case:

CASE I.

H. was admitted with a penetrating shell wound of the pelvis and fracture of the left ischium. A piece of shell had been removed with some fragments of bone before admission.

On April 14th the wound was drained and cleaned and two Carrel tubes inserted; 30 c.cm. Leclainche and Vallée serum were given, the bacteriological report being *B. perfringens*, streptococcus, *Vibrion septique*. The *x* rays showed no further foreign body.

On April 18th the patient still had fever, the wound was dirty, and gas bubbled out. Difficulty of micturition existed; 10 c.cm. anti-*Vibrion septique* serum were given and a further *x* ray photograph asked for. This showed a piece of shell near the bladder.

On April 28th the wound was opened up, the shell and some sequestra were removed with long forceps from the pelvis. The wound was cleaned and four Carrel tubes inserted; 20 c.cm. anti-*Vibrion septique* serum were given with 10 c.cm. Leclainche and Vallée. The patient had a septicaemic appearance (temperature 103°, pulse 140) with extreme anaemia.

On April 29th and on April 30th 10 c.cm. anti-*Vibrion septique* serum were given. The blood gave a pure culture of *Vibrion septique*, but a second examination on May 2nd was negative.

After a very protracted illness the patient recovered and was discharged on July 23rd in good condition.

During the period from March 21st to September 6th, anti-gangrenous serums were given preventively in 433 cases, all of a severe type, including nearly 300 fractures, many cases already presenting one or other of the clinical signs of gas gangrene, such as crepitation, discoloration of muscle, bronzing of skin, oedema, and bad odour. A large number were wounds of the lower limbs. Nearly all were received within the first twenty-four hours after being wounded. The serum was given subcutaneously in one pint of saline at the time of the operation. This dilution, it is believed, has averted the anaphylactic phenomena which have been observed in cases in which this method of procedure has not been followed.

SCOPE OF THE INQUIRY.

The investigations fall into three groups:

I.—222 cases (126 fractures): *Mélange* of 10 c.cm. each of anti-*perfringens*, anti-*Vibrion septique*, and anti-*oedematiens* serum of M. Weinberg.

II.—154 cases (110 fractures): 30 c.cm. of the polyvalent serum of MM. Leclainche and Vallée.

III.—57 cases (34 fractures): 30 c.cm. of *mélange* (serum of M. Weinberg) with 10 c.cm. of the polyvalent serum of MM. Leclainche and Vallée.

CLASS I.

(*a*) *Mortality.*—Where the *mélange* was given at or before the first operation, no case died from gas gangrene, although there were nineteen deaths out of the number from the effects of shock, from multiple fractures, haemorrhage, meningitis, or streptococcal septicaemia.

(*b*) *Amputation.*—In fourteen of these cases the serum was administered at the same time that amputation was performed for massive gas gangrene (it is difficult to draw the line between preventive and curative treatment). Of these fourteen cases, twelve recovered. The two fatal cases both died at the end of a fortnight from streptococcal septicaemia, all signs of gas gangrene having disappeared for more than a week.

(*c*) *Conservative Treatment.*—In a very large number of cases the administration of *mélange* has permitted conservative treatment to be adopted instead of the amputation which would otherwise have been inevitable; the following cases are examples:

CASE II.

B. was admitted with a penetrating shell wound of the right thigh, having been wounded in the night of August 3rd.

On admission, during the night of August 4th, the patient was in a condition of acute toxaemia. He was vomiting; the temperature was 102°, and the pulse 150. The right thigh was tense, pale, and swollen, and the veins were much dilated. Gas bubbled from the small entry wound on the inner side of the thigh.

The patient was brought into the theatre, and 60 c.cm. of *mélange* serum were given simultaneously with two pints of saline, followed by 30 c.cm. of camphorated oil, and a rectal saline containing sodium bicarbonate. Very large incisions were made in the thigh, and a piece of shell with infected cloth and gaseous infected muscle evacuated. Four Carrel tubes were inserted. The bacteriological report gave *B. perfringens* and the streptococcus from the shell. The blood culture was negative.

The patient made a good recovery.

CASE III.

P. (American) was wounded on July 19th at 8 a.m. in the left foot by a large piece of shell which traversed the tarsus causing complete disorganization. On admission at 5.30 p.m. the smell was most offensive, the outer half of the foot was open, and a mass of comminuted bone exposed. The foot was swollen. The bacteriological report gave *B. perfringens*, streptococcus, and bacilli with terminal spores.

The wound was cleaned, loose pieces of bone removed, Carrel tubes inserted, and 30 c.cm. *mélange* given subcutaneously.

On July 23rd the foot was swollen, and there was some fever. Further doses of *mélange* were given—60 c.cm. in all—and the patient made a very good recovery, with a useful foot.

CASE IV.

L. was wounded on July 18th at 8 a.m., and was suffering from the effects of haemorrhage from a large open shell wound of the right calf.

On admission at 5 p.m. on July 18th the patient was given subcutaneous saline, and 10 c.cm. of camphorated oil. The wound was then excised, 30 c.cm. of *mélange* serum being given subcutaneously. The bacteriological report gave *B. perfringens*, streptococcus, and spores.

The following day the wound was dirty, and still smelling very badly. Six Carrel tubes were arranged, and 20 c.cm. of anti-*perfringens* serum given.

On July 21st masses of dead muscle were cut away, but there were no general symptoms, and the patient made a good recovery in spite of the loss of calf muscle.

CASE V.

In another case, D. (a badly infected fracture), the use of serum was instrumental in saving the leg from amputation.

The patient was wounded on June 10th, and was admitted and operated on the same day. There was a badly comminuted fracture of the tibia and fibula. A large piece of shell was removed and drainage established by large incisions. There was bronzing of the skin, and amputation was considered; 30 c.cm. *mélange* was given.

On June 15th the muscle was much more swollen, there was gas in the deeper tissues, and the smell was foul. There was some oedema, but no crepitation of the skin. The same day all sequestra were removed and further incisions made. *B. perfringens*, *Vibrion septique*, and *B. putrificus* were reported.

Further doses of serum were given on June 16th and 18th. The patient made a good recovery with a fairly useful leg.

Disintoxication.

The value of this serum as a disintoxicating agent has been proved in several cases. Its administration has made it possible to wait for some hours until the condition of the patient has improved sufficiently to allow of surgical measures being employed, as in the following case:

CASE VI.

M. was wounded at 9 a.m. on August 19th. There was a penetrating wound of the thigh with fracture of femur. At 10 p.m. on August 22nd, excision of the wound, sequestrotomy with removal of bullet was performed. A Thomas splint was applied, and Leclainche and Vallée serum, 30 c.cm., given.

The following day there was rise of temperature and pulse, and a bacteriological report of *B. perfringens* from the wound. The wound was freely opened up and Carrel tubes inserted. At night the condition of the patient was very grave. There was great swelling of the thigh (temperature 105.6°, respirations 40), the pulse was uncountable and barely perceptible. A subcutaneous saline was given, with 30 c.cm. of *mélange* serum and 10 c.cm. of camphorated oil.

Early the following morning, though the thigh was enormously swollen, the patient was a little better. Amputation was performed above the seat of the fracture (circular with lateral incisions), while an intravenous saline was given; 30 c.cm. of *mélange* were given subcutaneously and 10 c.cm. of camphorated oil. The usual dressing of 5 per cent. salt and 2½ per cent. carbolic acid was applied. *B. perfringens* and a streptococcus were found in the wound.

The following day there was decided improvement (pulse 120, temperature 100°). A further dose of 30 c.cm. *mélange* serum was given, and on August 29th 20 c.cm. anti-*perfringens* serum.

The patient made an excellent recovery.

Infected cases, where *mélange* serum was omitted either by accident or from the meagre supply, have not done as well as others.

CASE VII.

R. There was a large perforating wound of the left arm with a comminuted fracture of the humerus by *bombe d'avion*. The artery was intact, but there was much destruction of muscle.

The patient was wounded on June 10th. The wound was excised on the following day. The bacteriological report was negative, and no serum was given. Four days later the arm was swollen and showed much yellow serosity in the wound. Large incisions were made and all sequestra removed. *B. perfringens* and *Vibrion septique* were reported. In the absence of anti-*perfringens* serum, a mixture of anti-*oedematiens* and anti-*Vibrion septique* was given.

On June 21st the arm was still much swollen, and the shoulder was also involved, a solid oedema running up along the course of the vessels. The bacteriological report gave *B. perfringens*, *B. putrificus*, spores, and streptococcus. Amputation in the upper third was performed. The biceps and coraco-brachialis muscles were infected in their whole length and were dissected out; 30 c.cm. of anti-*Vibrion septique* serum were given.

The patient made a good recovery.

CASE VIII.

P. There were multiple infected shell wounds, with several fractures, and a wound of the left popliteal vein. The patient was wounded on July 25th at 3.30 a.m., and was admitted and operated on the same evening. Numerous projectiles were removed, including a large superficial one from the right thigh. Unfortunately no serum was given. The following morning the patient presented a blanched appearance. In the early afternoon the right thigh began to swell, crepitation extending on to the abdomen. A high amputation was performed, gas bubbling from the divided muscles; 30 c.cm. of *mélange* were given, with two pints of saline intravenously at the time of operation, but had no effect on the ultimate issue, death taking place in a couple of hours. *B. perfringens* was isolated from the piece of shell and from the blood.

CLASS II.

In 154 cases (110 fractures) a trial was made under the same conditions of the polyvalent serum prepared by MM. Leclainche and Vallée, who kindly placed a sufficient quantity at my disposal. In 10 of these (all amputations), the ultimate result could not be ascertained as the patients, for military reasons, were evacuated within a few hours of operation.

(*a*) *Mortality.*—Of these 154 cases 19 were fatal—6 of the deaths being due to gas gangrene. Of the 6 fatal cases of gas gangrene 3 had also a concurrent streptococcal septicaemia.

(*b*) *Amputation.*—In 15 of the 154 cases amputation was performed for massive gas gangrene, with 11 recoveries and 4 fatal results. Of these fatal cases 2 were also associated with streptococcal septicaemia.

CASE IX.

In one of these cases the administration of 30 c.cm. of serum the day before amputation did not prevent the onset of gas gangrene. As the *B. oedematiens* was found in the wound (against which the serum Leclainche and Vallée does not protect), it is possible that the severe symptoms were due entirely to this organism. After the administration of *mélange* serum, the patient made a wonderful recovery. In his case oedema of the limb with toxaemia was the most prominent feature.

CASE X.

Le B. was wounded on August 31st by shell, receiving a penetrating wound of the right knee-joint with transverse fracture of the femur immediately above the condyles. Arthrotomy had been performed before admission by a horseshoe flap containing the patella. The limb was immobilized for transport in plaster.

On removing the dressing a very foul-smelling discharge was present, but there was no swelling. The bone was discoloured. The wound was cleaned and placed on a Thomas splint. The following day, September 10th, there was pyrexia; Carrel tubes were placed in the wound and 30 c.cm. Leclainche and Vallée serum were given subcutaneously in saline.

On September 11th there were symptoms of toxaemia. The temperature was 105°, pulse 140, and respirations 40. The patient was jaundiced and vomited brownish material several times at 8 p.m.

Amputation was performed above the fracture. There was no collection of pus in the knee-joint, but the fractured ends of the femur were extremely dirty, and there was general swelling of the thigh in the neighbourhood of the fracture. The bacteriological report was *B. perfringens* and steptococcus. The skin and cellular tissue of the abdomen at the site of the subcutaneous injections were swollen, and an incision was made, but only oedema found. On the following evening the amputation stump was enormously swollen, the swelling extending on to the buttock and lower abdomen. The patient was very ill and extremely yellow. The pulse was small, 144, and the temperature 101°. A large dose of serum was given, consisting of 10 c.cm. anti-*oedematiens*, 20 c.cm. anti-*Vibrion septique*, and 30 c.cm. anti-*perfringens* in subcutaneous saline. The patient was very restless and sleepless, and morphine, ½ grain, was given.

The following morning, to my surprise, the patient was still alive. There was still a great deal of oedema, and a red spot appeared on the inner side of the stump. Anti-*oedematiens* serum ran short, but on September 15th 20 c.cm. Leclainche and Vallée were given and 10 c.cm. of anti-*perfringens*.

On September 16th there was crackling in the abdominal wall, and multiple incisions were made, releasing greenish gaseous pus, which contained the streptococcus and *B. perfringens*; 20 c.cm. anti-*perfringens* serum with 20 c.cm. anti-*Vibrion septique* were given. The stump was rather less swollen.

On September 17th the general condition was better, but the pulse was still very rapid. The last 20 c.cm. of anti-*perfringens* serum were given. The laboratory reported the presence of *B. oedematiens* in the wound. I was fortunately able to secure more Weinberg serum during the afternoon, and 30 c.cm. of *mélange* were given in the evening. On the following day (September 18th) gas and pus poured out from the abductor muscles through the skin, which had given way; this persisted until September 20th, when 30 c.cm. *mélange* were again given.

On September 22nd, under an anaesthetic, the thigh was cleaned, masses of the necrotic adductor muscles washed out and the cavity well drained. On September 26th the wounds were healthy and all oedema had disappeared. The patient looked much healthier. the skin had lost its yellow tint. The pulse was still rapid.

Influence on Streptococcal Infection.

It was generally noticed during the period in which the Leclainche and Vallée serum was given preventively that, except in gas gangrene, the cases seemed to run a straightforward course, without severe streptococcal infections, and that secondary operations on this score were infrequent.

Among 15 cases of streptococcal septicaemia which occurred in patients admitted during this period, only four had received preventive doses of Leclainche and Vallée serum. Seven patients who had all been treated with fairly large doses of Leclainche and Vallée serum recovered.

CLASS III.

Believing that the Leclainche and Vallée serum might have an inhibiting action on the streptococcus, in a third series of cases (57, with 36 fractures) 10 c.cm. of Leclainche and Vallée serum were added to the initial dose of 30 c.cm. of *mélange* serum. Although in ten of these cases gangrene was already present in the form of cellulitis or abscess, in only one did massive gas gangrene develop—namely, after ligature of the external iliac artery, fifteen days after the preventive dose of *mélange* had been given.

CASE XI.

J. was wounded on September 2nd, at 4 p.m., a bullet perforating the left thigh and pubic ramus, fracturing the femur and pelvis, and reaching the pelvic peritoneal cavity.

At 9 p.m. on September 3rd the bullet was removed by laparotomy, the pelvis drained, and the thigh wound excised and drained (Carrel tubes). *B. perfringens* and the streptococcus were reported in the thigh wound; 30 c.cm. *mélange* and 10 c.cm. Leclainche and Vallée serum were given subcutaneously.

The patient did fairly well until September 15th, when some clots appeared in the thigh wound coming from the softened femoral artery near the point of division. Amputation was performed, followed by ligature of the external iliac immediately above Poupart's ligament. The patient bore the operation well, but in thirty-six hours gas gangrene (*B. perfringens* and streptococcus) occurred in the external thigh muscles, and death took place in a few hours.

(*a*) *Mortality.*—Two cases were fatal in this series, one already mentioned (Case XI, J.) and another who, after amputation for gas phlegmon associated with streptococcal osteomyelitis, died from intestinal obstruction due to old appendicitis.

(*b*) *Amputation.*—Although many of these cases have been badly infected fractures of the lower limb, only three have been amputated, one for streptococcal infection, two for secondary haemorrhage.

Not only has it been possible in these cases to adopt conservative lines in fractures of the diaphysis, but, in addition, wounds involving the articulations—hip, knee, shoulder, ankle, and tarsus—have run an unusually favourable course.

In secondary operations, where latent microbes in sequestra so often cause a disappointing result (secondary suture, reamputation, etc.), a preventive dose of Leclainche and Vallée serum and *mélange* has been found useful; and it is possible that its systematic use will make it possible to operate in such cases earlier than one would otherwise think safe, even with negative bacteriological findings. There is a tendency for anaërobic infection to linger in sequestra for a surprisingly long interval.

CASE XII.

B. In May, 1917, a gas abscess came under my care. The patient had been wounded in September, 1914, by a bullet with fracture of the femur; he lay for five days without dressing, and the thigh was badly infected. Recovery took place, and the man was discharged from the army in May, 1915.

Working as a wood-cutter in the neighbourhood of the Scottish Women's Hospital (Hôpital Auxiliaire d'Armée 30) for some days, he noticed that his thigh was swollen. There was no history of recent injury. The leg was fomented; the night before admission one of the old scars gave way with some relief.

On admission the patient was jaundiced, with dry furred tongue. There was much swelling of the thigh. Gas bubbles exuded from the posterior scar, and a dark anchovy-coloured discharge. A large foul-smelling sequestrum was in the mouth of the wound. The adductor muscles were swollen and infected. The *x*-ray photograph showed gas in the thigh and many small fragments of bullet.

The abscess was thoroughly drained, and gangrenous muscle cut away. From the sequestrum *B. perfringens*, *B. sporo enes*, and *B. oedematiens* were identified. The latent period exceeded two and a half years.

CONCLUSIONS.

1. That the administration of a powerful anti-gangrenous serum such as that of MM. Weinberg and Séguin is of real value in preventing the incidence of gas gangrene, not replacing but assisting surgical treatment.

2. That employed as a curative agent in cases of advanced infection it is a disintoxicating agent of great value if used in sufficient quantities.

3. That the polyvalent serum of MM. Leclainche and Vallée has a marked influence on the after-history of the cases with coincident streptococcal infections.

4. That the dilution of the serum by normal saline solution and its subcutaneous administration has made anaphylactic phenomena extremely rare.

5. That in cases where the special microbe can be isolated, or in blood infections, the appropriate serum can with advantage be pushed. The length of time necessary for these examinations makes it wiser to give the *mélange*, especially in cases where sporulated bacilli are present in the original bacteriological preparations.

6. That before secondary operations in infected cases a further dose should be administered by preliminary fractional dose.

REFERENCES.

[1] *Proc. Roy. Soc. Med.*, Lond., vol. x, pp. 29-110. [2] *Presse méd.*, August 29th, 1918.

ON THE TREATMENT OF PNEUMONIA.

A SERIES OF 67 CASES WITH 2 DEATHS.

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THE problem of pneumonia for the general practitioner is the same to-day as it has been for many years. It is still the "Captain of the men of Death," and it is one of the few diseases in which advance in knowledge, and therefore in treatment, cannot be made by the general practitioner. Its invasion is too sudden for specific prevention, its symptomatology and clinical manifestations are the most self-evident of all diseases, and its morbid anatomy is well known. The recent bacteriological advances, with the differentiation of four types of pneumococci, are scarcely for the man at the cross-roads. And so, pending the development of a real scientific treatment, probably of the vaccine variety, we are still, as of yore, dependent on what is truly, and perhaps medico-humorously, named "expectant" treatment. This gives great play to individual fancy, and hence we find recorded an almost infinite variety of remedies in pneumonia. In spite of all, the mortality to-day is, speaking generally, the same as it has always been in the past.

Yet it seems to me that there is one principle in the treatment of pneumonia which is not appreciated to the full, and on which enough stress is not laid in the textbooks, and that is *the enormous importance of rest.* One of the chief dangers in pneumonia is cardiac failure, and I have never forgotten seeing, while an undergraduate, a patient with pneumonia sat up in bed for examination, and laid back dead. That was an extreme illustration of the failure to carry out the principle of rest, and it is also evidence for the second great principle in the treatment, which *is* laid down more fully in textbooks—"to support the circulation."

While in charge of medical wards at a general hospital in France for twelve months, I had under my care sixty-seven cases of acute lobar pneumonia. Of these only two died, a mortality of 3 per cent. The mortality in the hospital area for the same period, *including my cases*, was 12 25 per cent. My cases were not, of course, selected in any way, most being admitted as local sick.

They were all treated on the same principles, with variations and additions as necessity arose. I first heard these principles laid down by Professor Greenfield, Professor of Pathology in Edinburgh University, ten years ago, and I have adopted them ever since. There are two essential parts of the treatment.

1. After the diagnosis has been definitely made, the patient is kept *absolutely at rest;* especially is he not allowed to sit up on any account or for any purpose, nor even to turn himself in bed without assistance. I make no further physical examination of the chest until after